

# **EXHIBIT 26**



Managing:

# Pain

with

## Appropriate Use of Opioids

Version 1.0

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**Table 1. Pain Assessment****Checklist****History**

- Pain
  - Location (may be multiple)
  - Category (see Table 2)
  - Intensity (see Table 3)
  - Course: onset, duration, fluctuation, rhythms, aggravating/alleviating factors
  - Etiology: primary disease/condition, therapy/procedure, comorbidities
- Effects of pain on patient
  - Impaired functioning (physical, mental), quality of life
  - Accompanying symptoms (e.g., nausea, impaired sleep, loss of appetite, decreased activity)
  - Emotional distress (e.g., crying, angry, anxious, depressed, suicidal)
  - Impaired relationships (e.g., family, school, occupational, social)
- Special issues
  - Psychiatric or substance abuse history
  - Patient/family/significant others' knowledge and beliefs about pain
  - Communication barriers; minority/cultural factors
  - Litigation or worker's compensation
- Special populations (e.g., pediatric, geriatric, pregnancy/lactation, substance abuse/addiction, cognitive impairment)

**Relevant laboratory and imaging studies based on data from patient history and examination**

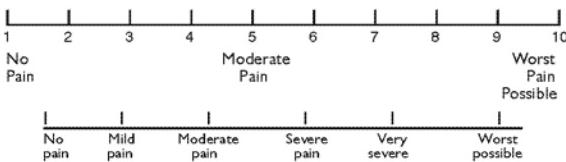
**Table 2. Categories of Pain\***

- **Acute (eudynia):** usually related to an identifiable trauma or medical condition; resolution within days or weeks as condition resolves.
- **Chronic (maldynia):** may/may not be related to identifiable pathology; may persist indefinitely; frequently associated with mood disturbances, physical dysfunction, social disruption.
- **Neuropathic:** acute or chronic pain resulting from peripheral or central nervous system pathology; described as sharp, shooting, tingling, and/or burning, electric; often associated with neurological deficits.
- **Nociceptive:** acute or chronic pain related to tissue damage, involving direct stimulation of intact nociceptors, and relayed along normally functioning nerves.
- **Somatic (from skin, soft tissue, muscle, bone):** sharp/stabbing, aching, and/or throbbing pain—easily localized.
- **Visceral (from internal organs):** gnawing, cramping, deep, and/or pressing pain difficult to describe and localize; may be concurrent nausea, vomiting, or diarrhea.

\*In documentation, use patient's own words to describe pain.

Adapted from: Emanuel LL, von Gunten CF, Ferris FD. The Education for Physicians on End-of-Life Care (EPEC) curriculum. Module 4, Pain Management. *EPEC Participant's Handbook*. EPEC Project. Princeton, NJ: The Robert Wood Johnson Foundation; 1999.

MNK-T1\_0002248919



From: Acute Pain Management: Operative or Medical Procedures and Trauma, Clinical Practice Guideline No. 1, AHCPR Publication No. 92-0032; February 1992. Agency for Healthcare Research & Quality, Rockville, MD; pages 116-117.

#### NO PAIN

MILD PAIN (you know it's there but hardly notice it)

MODERATE PAIN (a little more pain than mild pain — it does not stop you from doing things)

SEVERE PAIN (wakes you from sleep or makes you stop your activity to ease the pain)

VERY SEVERE PAIN (you cannot stand the pain and are unable to do any activity or sleep)

WORST POSSIBLE PAIN (the worst pain you can imagine)

- Reassess at specified intervals and with same scale to evaluate intended effect of therapy.
- Therapeutic goal is satisfactory pain control (usually below 4) with tolerable side effects and acceptable quality of life (physical, psychological, occupational, social functioning).

**Table 4. Addiction Assessment Tools**

#### CAGE-AID (CAGE Adapted to Include Drugs)\*

- Have you felt you ought to Cut down on your drinking/drug use?      1 Yes      0 No
- Have people Annoyed you by criticizing your drinking/drug use?      1 Yes      0 No
- OR
- Have people told you about things you said/did while you were drinking/on drugs that you could not remember (Amnesia)?      1 Yes      0 No
- Have you ever felt bad or Guilty about your drinking/drug use?      1 Yes      0 No
- Have you ever needed a drink/used drugs as an Eye-opener or to steady your nerves first thing in the morning?      1 Yes      0 No

TOTAL SCORE OF  $\geq 2$  CONSIDERED CLINICALLY SIGNIFICANT.

#### SISAP (Screening Instrument for Substance Abuse Potential)

For predicting addiction risk in patients receiving opioids.

Access at: [http://www.stoppain.org/pcd/\\_pdf](http://www.stoppain.org/pcd/_pdf).

#### DAST-20 (Drug Abuse Screening Tool)

For detecting potential drug abuse or dependency disorders in patients.

Access at: <http://www.adai.washington.edu/instruments/pdf/DAST.pdf>

#### ORT (Opioid Risk Tool)

For predicting patients at high and low risk for opioid-related aberrant behavior.

Access at: <http://www.lifetree-research.com/media/articles/ORT.pdf>

#### SOAP (Screener and Opioid Assessment for Patients in Pain)

For chronic pain patients being considered for long-term opioid treatment.

Access at: <http://www.painedu.org/soap.asp>.

\*Adapted from: Brown RL, Rounds, LA. Conjoint screening questionnaire for alcohol and drug abuse. Wis Med J 1995;94:135-140.

- Critical to distinguish tolerance, dependence, and pseudo-addiction from addiction (see Table 7).

#### Acute Pain (eudynia)

- Establish diagnosis and treat underlying conditions.
- Determine associated pain location, intensity, and category (see Tables 1, 2, 3).
- Symptomatic treatment of acute pain should be multimodal, with possible application of:
  - Non-pharmacologic approaches (e.g., heat, ice, rest, massage, education)
  - Non-opioids (e.g., ASA, APAP, NSAIDs, COXIBs)
  - Opioids titrated to effect (see Table 9).
  - Use least invasive route of administration.
  - Treat pain before it becomes severe; dose PRN.
  - Risk of addiction rare (see Table 7).

#### Chronic non-cancer pain (maldynia)

- Establish diagnosis and treat underlying conditions.
- Patients may be considered for therapeutic trial of opioids.
- Complex patients (e.g., addiction, medical problems, psychopathology, rehabilitation issues) may need management in specialty setting.
- Written treatment plan (individualized to patient and pain problem) includes:
  - Medication(s) (name, dose, frequency)
  - Measurable objectives (clinical outcomes)
  - Informed consent (risks/benefits of opioid therapy)
  - Physician-patient therapeutic agreement (terms/conditions for prescribing opioids)
- Prepare exit strategy for patients failing to meet specific goals of agreed-on therapy.

#### Cancer-related pain

- Establish diagnosis and treat underlying conditions.
- Patients may be more tolerant of opioid risks and side effects.
- Pain prevention easier than relieving existing pain — for chronic pain, dose ATC with fixed dose, plus PRN doses for breakthrough pain.
- Appropriate opioid dose can relieve pain throughout dosing interval without unmanageable side effects — single-entity opioids have no maximum dose but may be limited by side effects.
- Anticipate certain opioid-induced side effects by beginning prophylactic medication when initiating opioid therapy (see Table 6).

#### Rescue dose for breakthrough pain

- Divide standing dose by hourly frequency of standing dose; e.g., 60 mg morphine sulfate (MS) PO q 4 h:  $60 \div 4 = 15$  mg MS q 1 h PRN
- Use same drug as standing drug. If not possible, use equianalgesic dose of same class of drug (see Table 9).
- Alternative: 10 - 15% of 24 h (ATC + PRN) dosage PO q 1 - 2 h PRN.
- If rescue dose required regularly (in each dosing interval) for  $> 24$  h:
  - Increase standing dose by quantity of rescue dose given in dosing interval; e.g., 60 mg MS PO q 4 h with two 15 mg rescues in average 4-h period:  $60 \text{ mg} + 30 \text{ mg} = 90 \text{ mg MS q 4 h}$ ;
  - Increase rescue dose:  $90 \div 4 = 22$  mg MS (elixir) q 1 h PRN.

#### ALL PATIENTS

- Periodic review
- Pain rating (intensity, category, location)
- Treatment effectiveness (goal established on 0 - 10 pain intensity scale)
- Patient's functional changes
- Side effects/adverse effects
- Patient adherence to regimen
- Diligently documented medical records include:
  - Patient visits
  - Specialty consults
  - Therapeutic/diagnostic procedures, lab results
  - Prescriptions (e.g., date, drug, strength, dosage units, route of administration, frequency)
  - Document the 4 A's (Analgesia, Activity, Adverse Side Effects, and Aberrant Behavior)\*

\* Passik SD, Weinreb HJ. Managing chronic nonmalignant pain: overcoming obstacles to the use of opioids. Adv Ther. 2000;17:70-83.  
Passik SD, Kirsh KL, Whitcomb L, et al. Pain clinicians' rankings of aberrant drug-taking behaviors. J Pain Palliat Care Pharmacother. 2002;16:39-49.

Adapted from: Model Guidelines for the Use of Controlled Substances for the Treatment of Pain. Eustis, TX: Federation of State Medical Boards of the United States, Inc.; 1998. Pocket Guide for Pain Management in Adults. Boston, MA: Tufts-New England Medical Center; 1998. Scott CJ, Griffin CB, eds. Pain Management Tables and Guidelines: Pain and Symptom Management. Boston, MA: Brigham and Women's Hospital; 2000.

**Table 6. Management of Opioid Side Effects**

Case: 1:17-md-02804-DAP Doc #: 2251-26 Filed: 08/13/19 4 of 9. PageID #: 350796

Adverse Effect	Management
Confusion/Delirium	<ul style="list-style-type: none"> <li>Assess for other causes (e.g., other psychoactive agents, CNS pathology); check electrolytes, calcium, glucose</li> <li>Consider metabolic accumulation</li> <li>Consider adding non-opioid analgesic or consult specialist for interventional technique to achieve opioid dose reduction</li> <li>Consider changing opioid (See Table 8)</li> <li>Consider neuroleptic agent (e.g., olanzapine, risperidone)</li> </ul>
Constipation (begin bowel regimen at onset of opioid therapy; goal is frequency/quality of movement acceptable to patient; tolerance does not develop)	<ul style="list-style-type: none"> <li>Increase fluids; exercise (when appropriate)</li> <li>Initiate stimulant laxative* (e.g., senna, casanthranol) + stool softener (docusate) taken at fixed daily dose; consider increasing laxative dose when increasing opioid dose (opioid constipation is dose dependent)</li> <li>Consider adding non-opioid analgesic to allow opioid dose reduction</li> <li>Rectal examination to check for impaction; if found, disimpact</li> <li>Consider adding another agent (e.g., magnesium hydroxide, bisacodyl, rectal suppository, lactulose, sorbitol, magnesium citrate; Fleet, saline, or water enema) when needed</li> <li>Consider prokinetic agent (e.g., metoclopramide)</li> </ul>
Nausea/Vomiting (prescribe antiemetics with initial opioid prescription; tolerance may develop)	<ul style="list-style-type: none"> <li>Assess for other causes (e.g., constipation/obstruction, CNS pathology, chemotherapy, radiation therapy)</li> <li>Antiemetic ATC for few days to 1 week, then PRN (e.g., prochlorperazine, thiethylperazine, metoclopramide, droperidol, ondansetron, haloperidol)</li> <li>Consider adding non-opioid medication to achieve opioid dose reduction</li> <li>Consider changing opioid or route of administration</li> </ul>
Pruritis	<ul style="list-style-type: none"> <li>Consider antihistamine (e.g., diphenhydramine, cetirizine, fexofenadine, doxepin)</li> <li>Consider switching opioids</li> </ul>
Respiratory depression, hypoventilation (tolerance often develops with chronic use)	<ul style="list-style-type: none"> <li>If respiratory rate falls below 10, shallow breathing, or unresponsive to voice/stimulation, as appropriate:           <ul style="list-style-type: none"> <li>Consider comfort measures if patient is terminal and DNR</li> <li>Assure patient airway; initiate supportive respiratory measures (e.g., jaw lift, AMBU bag) – if patient is not terminal or DNR</li> <li>Consider naloxone if life-threatening: dilute 0.4 mg naloxone with 9 mL saline and administer in 0.04 (1 mL) increments until respiratory rate &gt; 8 – 10/min; use cautiously to avoid withdrawal symptoms and severe pain</li> <li>Hold further doses of opioids until episode resolves</li> </ul> </li> </ul>
Sedation (tolerance often develops with chronic use)	<ul style="list-style-type: none"> <li>Assess degree of sedation, and as appropriate:           <ul style="list-style-type: none"> <li>Assess for other causes (e.g., other psychoactive agents, hypercalcemia, CNS pathology, metastases, sepsis)</li> <li>Consider addition of caffeine, methylphenidate, dextroamphetamine, modafinil</li> <li>Consider titrating opioid dose downward to reduce sedation (if pain control can be maintained)</li> <li>Consider non-opioid analgesic to achieve opioid dose reduction</li> <li>Consider lower opioid dose administered – consistent with duration of action – could drive prescribing q 8h</li> <li>Consider changing opioid</li> </ul> </li> </ul>

\*If long-term use anticipated, use cautiously because of possibility of dependence.

Adapted from: Use of Opioid Analgesics for the Treatment of Chronic Noncancer Pain—A Consensus Statement and Guidelines. Canadian Pain Society; 1998. Cherny N, Ripamonti C, Pereira J, et al for the Expert Working Group of the European Association of Palliative Care Network. Strategies to manage the adverse effects of oral morphine: an evidence-based report. *J Clin Oncol* 2001;19:2542–2554. McNicol E, Horowicz-Mehler N, Fisk RA, et al. Management of opioid side effects in cancer-related and chronic noncancer pain—a systematic review. *J Pain* 2003;4:231–256.

**Table 7. Analgesic Tolerance, Dependence, Addiction**

Term	Definition	Comments
Tolerance	Neuroadaptation to effects of chronically administered opioids, requiring increasing doses to maintain analgesia or decreasing analgesia over time.	<ul style="list-style-type: none"> <li><i>Not in itself</i> predictive/diagnostic of addiction</li> <li>Treatment not required if dose stabilizes</li> <li>Treatment includes changing opioids or adding non-opioid analgesic modalities</li> <li>Dosages must be increased to produce the same effect</li> </ul>
Physical dependence	Physiologic state in which abrupt cessation of opioid, or administration of opioid antagonist, results in withdrawal syndrome: e.g., agitation, tachycardia, hypertension, piloerection, coryza, tremors, sweats, chills, lacrimation, abdominal cramps, arthralgia, myalgia, vomiting, diarrhea, increased pain.	<ul style="list-style-type: none"> <li><i>Not in itself</i> predictive/diagnostic of addiction</li> <li>Common state with long-term opioid therapy</li> <li>Treatment not needed for physical dependence</li> <li>Absstinence requires treatment</li> <li>Withdrawal may be avoided by tapering down opioid therapy</li> </ul>
Addiction	Persistent psychological pattern of inappropriate opioid use despite harm to self and others; e.g., compulsive preoccupation with obtaining/using opioids, loss of control over opioid use, lack of concern for adverse consequences of opioid misuse.	<ul style="list-style-type: none"> <li>Screen patient for risk factors (see Table 4)</li> <li>Review patient medication history</li> <li>Document and evaluate aberrant drug-taking behavior (e.g., chronic early refills, prescription loss, unauthorized dose escalation)</li> <li>Patients with substance abuse/addiction disorders potentially at higher risk for opioid abuse but can be treated with opioids under controlled circumstances; may require specialty referral</li> <li>Addiction treatment requires referral to addiction specialist</li> </ul>
Pseudoaddiction	Drug-seeking behavior focused on pain relief, due to undertreatment of pain.	<ul style="list-style-type: none"> <li>Behavior normalizes with adequate analgesia</li> </ul>

**Table 8. Opioid Equianalgesic Conversion**

<ul style="list-style-type: none"><li>• After optimum titration of dose/frequency, consider changing opioid if:<ul style="list-style-type: none"><li>◦ Unachieved control of pain</li><li>◦ Inadequate onset/duration of action</li><li>◦ Intolerable side effects</li><li>◦ Unsatisfactory route of administration</li><li>◦ Unacceptable drug-drug interaction</li><li>◦ Dissatisfaction of patient</li></ul></li></ul>	
• Step 1	First determine total 24 hour dose of current drug. Locate the dose of the present opioid by the present route listed in the equianalgesic chart (Table 9). Then determine the number of equianalgesic dose units in the 24-hour dose.
• Step 2	Locate the dose of the new opioid by the present route listed on the equianalgesic chart (Table 9)
• Step 3	Determine the 24-hour dose of the new opioid by multiplying the equianalgesic dose units of the present opioid.
• Step 4	Divide the 24-hour dose of the new drug by the number of doses to be given each 24 hours.
• Formula:	Current total 24-h opioid dose X Equianalgesic conversion factor for new opioid = Dose of the new opioid every 24 hours Equianalgesic conversion factor for current opioid
<ul style="list-style-type: none"><li>• Key Considerations<ol style="list-style-type: none"><li>1. All equianalgesic ratios/formulas are approximations; clinical judgment is needed when making dose or drug conversions.</li><li>2. If the patient is opioid tolerant and has been taking a high dose of opioid, it is best not to abruptly discontinue the present opioid and convert to the new in one step. This could lead to an overdose, causing undesirable side effects, or an under dose, precipitating severe pain. Instead, in these cases, make the transition starting with 50% of the current opioid dose combined with 50% of the projected dose for the new opioid. Gradual increases in the new opioid drug and decreases in the old can be made until the switch is complete over a period of several days. It may be necessary to adjust the dose of the new opioid (ie, maintain the 50% dose of the old opioid and increase the new opioid for insufficient pain relief). Once the combined doses provide good pain control, drop the old opioid and double the new.</li></ol></li></ul>	

Adapted from: Pain, 2nd Edition - Clinical Manual, Margo McCaffery, RN, MS, FAAN; and Chris Pasero, RN, MSNc

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**Table 9. Opioid Analgesics****Drugs in red are long acting, controlled-release, or long half-lived.**

Drug Generic/Brand	INJ	:	PO	Usual Adult Dose	Dose Adjustment	Clinical Comments
<b>MU AGONISTS COMMONLY USED FOR MILD TO MODERATE PAIN</b>						
<b>Tramadol</b> <i>Ultram</i>	NA		50 – 100 mg	PO: 50 – 100 mg q 4 – 6 h Max: 400 mg/d	Lower doses for medically ill and older patients	<ul style="list-style-type: none"> <li>Action analogous to synthetic codeine; partial non-opioid mechanisms of action (antidepressant-like)</li> <li>Caution if seizure risk</li> <li>Not a scheduled product</li> <li>Drug interaction with SSRIs and MAOIs</li> </ul>
<i>Ultram ER</i>	NA			PO: 100 mg/d initially, increasing in 100 mg increments q 5 d to max 300 mg/d		
<i>Ultracet</i> (with APAP)	NA			PO: 75 mg q 4 – 6 h prn Max: 300 mg (2.6 g APAP)/d ≤ 5 d		
<b>MU AGONISTS COMMONLY USED FOR MODERATE TO SEVERE PAIN</b>						
<b>Fentanyl [C II] (0.1 mg = 100 µg)</b> <i>Actiq</i>	NA			Lozenge: 200 µg q 30 min prn titrated increase	Geriatrics: Titrate with caution	<ul style="list-style-type: none"> <li>Lozenge for breakthrough cancer pain in patients taking ≥ 50 mg of another opioid</li> <li>Good choice if renal failure</li> <li>Patch for chronic pain, not for acute, postoperative pain, or mild/intermittent pain</li> <li>Buccal tablet for breakthrough cancer pain in opioid-tolerant patients</li> <li>Fentanyl-induced thoracic rigidity (FTR) seen with rapid IV administration</li> </ul>
<i>Duragesic</i>			NA	Patch: 25 µg/h q 72 h (transdermal 25 µg/h = 50 – 60 mg/24 h oral morphine)		
<i>Fentora</i>	NA			Buccal tablet: 100 µg q 30 min prn, titrated in 100 µg increments		
<b>Hydrocodone [C III]</b> <i>Lorcet HD, Lortab, Vicodin, others with APAP; Lortab ASA, Panasal, others (with ASA); Vicoprofen (with ibuprofen)</i>	NA		5 – 20 mg	PO: 5 – 10 mg q 4 – 6 h Max: 4 g/d of APAP or ASA, or 3.2 g/d of ibuprofen	Geriatrics: PO 2.5 – 5 mg q 4 – 6 h	<ul style="list-style-type: none"> <li>Equianalgesic to oral morphine</li> <li>Metabolite is hydromorphone</li> </ul>
<b>Hydromorphone [C II]</b> <i>Dilaudid</i>	1.5 mg	5	7.5 mg	PO: 1 – 4 mg q 4 – 6 h IV: 0.5 – 2 mg q 2 – 3 h IM/SC: 1 – 4 mg q 4 – 6 h Rectal: 3 mg q 6 – 8 h	Geriatrics: PO 1 – 2 mg q 4 – 6 h IV 0.5 – 1 mg q 4 – 6 h	<ul style="list-style-type: none"> <li>Infusion at rates &gt; 50 mg/h associated with myoclonus due to accumulation of hydromorphone-3-glucuronide</li> </ul>
<b>Levorphanol [C II]</b> <i>Levo-Dromoran</i>	2 mg	1	2 mg (acute) 1 mg (chronic)	PO: 4 mg q 6 – 24 h SC: 1 – 2 mg q 6 – 8 h	Geriatrics: May accumulate	<ul style="list-style-type: none"> <li>Doses are for single dose administration, not repeated dosing</li> <li>Availability uncertain</li> </ul>
<b>Methadone [C II]</b> <i>Dolophine, Methadose, generics</i>	10 mg	.5	5 mg	PO: 5 mg q 6 – 8 h IV: 10 mg q 6 – 8 h	Geriatrics: May accumulate	<ul style="list-style-type: none"> <li>For chronic pain</li> <li>May be more potent than equianalgesic potency listed</li> <li>Access for significant drug reactions</li> </ul>
<b>MORPHINE [C II]</b> <i>Avinza, Duramorph, Kadian, MS Contin (MSC), MSIR, Roxanol, others</i>	10 mg	3	30 mg (chronic) 60 mg (acute)	PO: 10 – 30 mg q 3 – 4 h (MSC 30 – 60 mg q 12 h) (Avinza 30 mg q 24 h) (Kadian 10 – 20 mg q 12 – 24 h) IV: 2 – 10 mg q 2 – 4 h SC: 5 – 20 mg q 4 h IV/SC: infusion 0.8 – 10 mg/h up to 80 mg/h IM: 5 – 20 mg q 4 h Rectal: 10 – 20 mg q 4 h	Geriatrics: PO 10 – 30 mg q 4 – 6 h (MSC 15 – 30 mg q 8 – 12 h) IV 2 – 10 mg q 4 – 6 h	<ul style="list-style-type: none"> <li>Different controlled-release preparations not interchangeable</li> <li>Morphine-3- and morphine-6-glucuronide may accumulate with chronic use, especially in renal failure</li> <li>May be more toxic in women, due to preferential-mediated metabolism use of glucuronidation* (estrogen-mediated metabolism)</li> </ul> <p>* Advances in Opioid Analgesics: Maximizing Benefit While Minimizing Risk; 2007.B. Eliot Cole, MD, MPA</p>

Oxycodone [C II] OxyContin Oxy IR Percolone, Roxicodone, others Percocet, Roxicet, others (with APAP); Percodan, Roxiprin, others (with ASA)	NA		PO: 10 mg q 12 h PO/ER: 5 mg q 6 h prn PO: 10–30 mg q 4 h PO: 1 tablet q 6 h Max: 4 g/d of APAP or ASA	Geriatrics: Use caution IN table C-II, in minor rescue dosage	
Combunox (with ibuprofen)	NA	5 mg	PO: 1 tablet Max: 4 tablets/24 h for 7 d		• For short-term ( $\leq$ 7d) management of acute pain
Oxymorphone [C II] Numorphan	1 mg	10	10 mg (rectal)	IV: 0.5 mg initially SC/IM: 0.5 mg initially, 1 – 1.5 mg q 4 – 6 h Rectal: 5 mg q 4 – 6 h	• 5 mg rectal suppository = 5 mg IM morphine
Opana	NA		10 mg	PO: 10 – 20 mg q 4 – 6 h	• For moderate to severe acute pain
Opana ER	NA		10 mg	PO: 5 mg q 12 h initially, titrate at 10 mg q 12 h q 3 – 7 d	• For moderate to severe chronic pain
<b>PARTIAL MU AGONISTS</b>					
Buprenorphine [C V] Buprenex	0.3 mg	NA		IM/IV over 2 min: 0.3 mg q 6 h prn Repeat 1x (0.3 mg) in 30 – 60 min if needed	• May precipitate withdrawal symptoms in patients physically dependent on mu opioids • Partially reversed by naloxone; use cautiously in respiratory-compromised patients
<b>KAPPA AGONISTS/MU ANTAGONISTS (analgesia limited by dose-related ceiling effect; concurrent use with mu agonists may precipitate abstinence/withdrawal symptoms)</b>					
Butorphanol [C IV] Stadol NS	2 mg	NA		IV: 0.5 – 2 mg q 3 – 4 h IM: 1 – 4 mg q 3 – 4 h NS: 1 mg (1 spray in 1 nostril), another 1 mg in 30 – 60 min if needed; may repeat dose sequence in 3 – 4 h	• Generally used as nasal spray • Use with pure agonist can result in withdrawal symptoms and seizures • Not recommended for long-term use • Has psychomimetic effects; elderly more likely to suffer from hallucinations and confusion • Partially reversed by naloxone
Nalbuphine Nubain, generics	10 mg	NA		IM/IV/SC: 10 mg/kg q 3 – 6 h Max: 20 mg/dose, 160 mg/d	• Use with pure agonist can result in withdrawal symptoms and seizures • Not recommended for long-term use • Elderly more likely to suffer from hallucinations and confusion • Partially reversed by naloxone

**NOTE:**

- SEE PRODUCT LABELING FOR COMPLETE PRESCRIBING INFORMATION.
- Any CNS depressant, including alcohol, can increase an opioid's effect and should not be used in conjunction with an opioid.
- Substantial interindividual variability in patient sensitivity to analgesic effects of opioids.
- Geriatric: Analgesic CNS side effects may be particularly prominent, especially with polypharmacy. Referral for interventional techniques often helpful.
- Opioids should be used cautiously in patients with impaired respiration, bronchial asthma, increased intracranial pressure, and renal and/or hepatic impairment.

**Routes of Administration (consider indication and/or availability):**

- Buccal/sublingual: easy to use, rapid absorption, alternative if swallowing is problematic.
- IM: painful administration, wide fluctuation in absorption, rapid falloff of action.
- Intraspinal (neuraxial or subdural and epidural): useful to enhance benefit to side effect ratio, especially if intractable lower-body pain or intolerable side effects with other routes; co-administration of non-opioid with opioid analgesic(s) can achieve profound analgesia without motor, sensory, or sympathetic blockade.
- IV: bolus most rapid onset of action, infusion slower onset and peak effect, steady blood levels.
- PCA: infusion pump allows patient control over pain experience, adjusts for variations in therapeutic response.
- PO: convenient, flexible, no skin puncture and risk of infection, steady blood levels.
- Rectal (suppository): alternative if PO unacceptable.
- Transdermal: easy to use; steady absorption; few side effects.

**Table 10. Risk Management Strategies to Minimize Medication Abuse and Enhance Patient Monitoring**

- Formal written agreement with patient, after detailed consent discussion, outlining clinician's policy for:
  - Providing controlled prescription drug;
  - Consequences of problematic drug-related behavior;
  - Criteria for exiting opioid therapy.
- Obtain all prior health records and permission to contact healthcare providers prior to prescribing.
- Prescription of long-acting drug in appropriate quantities for specific duration of time.
- Prescription of rescue medication not to exceed more than 2 doses in 24 hours.
- Only one specified pharmacy to fill prescriptions, with permission to contact.
- No early refills and no replacement of lost prescription without documented/confirmed loss.
- Frequent patient appointments, bringing filled prescriptions for unannounced pill counts.
- Baseline urine drug screen followed by unannounced future screens.
- Require non-opioid therapies as determined, including psychotherapy or referral to addiction medicine specialist if patient at risk or exhibits aberrant behaviors.
- Permission for others (e.g., spouse, family, friends) to give feedback to physician; consider sincerely expressed concerns.
- In states with electronic prescription monitoring/tracking, initial query of database and at regular intervals; respond/follow-up any unsolicited report

After: Fine PG, Portenoy RK. A Clinical Guide to Opioid Analgesia. New York: McGraw-Hill Company, Inc., 2004.

**Some Online Resources for Pain Management Information**

- Alcohol and Drug Abuse Institute Library, University of Washington <http://lib.adai.washington.edu>
- Agency for Healthcare Research and Quality (AHRQ) <http://www.ahrq.gov>
- American Academy of Pain Medicine <http://www.painmed.org>
- American Pain Foundation <http://www.painfoundation.org>
- American Pain Society <http://www.ampainsoc.org>
- American Society of Addiction Medicine <http://www.asam.org/>
- Chronic Pain Network <http://www.chronicpain.network.com>
- Beth Israel-Pain Medicine & Palliative Care <http://www.StopPain.org>
- Drug Enforcement Administration <http://www.usdoj.gov/dea>
- Emerging Solutions in Pain <http://www.emergingsolutionsinpain.com/>
- Federation of State Medical Boards of the United States <http://www.medsch.wisc.edu/painpolicy/>
- Institute for Clinical Systems Improvement (ICSI) <http://www.icsi.org>
- International Association for the Study of Pain <http://www.iasp-pain.org/>
- Johns Hopkins-Center for Cancer Pain Research/Pain Site <http://www.cancerpain.jhmi.edu/>
- Joint Commission on Accreditation of Healthcare Organizations (JCAHO) <http://www.jcaho.org/>
- Mayo Clinic Pain Management Center <http://www.mayoclinic.com/findinformation/diseasesandconditions/index.cfm>
- MD Anderson Pain Site <http://www.mdanderson.org/topics/paincontrol/>
- MEDLINEplus: Pain <http://www.nlm.nih.gov/medlineplus/pain.html>
- National Foundation for the Treatment of Pain <http://www.paincare.org/>
- National Initiative for Pain Control (NPIC) <http://www.painedu.org/npic.asp>
- National Pain Education Council <http://www.npecweb.org/>
- National Pain Foundation <http://www.NationalPainFoundation.org>
- Pain.com <http://www.pain.com>
- Pain EDU <http://www.painedu.org>
- Pain and Policy Studies Group <http://www.medsch.wisc.edu/painpolicy/>
- Partners Against Pain <http://www.partnersagainstpain.com>
- Practitioners' Manual (2006), Informational Outline of Controlled Substances Act <http://www.deadiversion.usdoj.gov/pubs/manuals/index.html>
- Substance Abuse and Mental Health Services Administration (SAMHSA) <http://www.kap.samhsa.gov>
- TALARIA: Hypermedia Assistant for Cancer Pain Management <http://www.talaria.org/>

## Drug Abbreviations

**APAP** acetaminophen (N-acetyl-p-aminophenol)

**ASA** acetylsalicylic acid

**COXIB** cyclooxygenase selective inhibitor

**MAOI** monoamine oxidase inhibitor

**NSAID** non-steroidal anti-inflammatory drug

**PCA** patient-controlled analgesia

**SSRI** selective serotonin reuptake inhibitor

**Do not print this panel**

## Disclaimer

Opioids have been shown to be a proper and effective treatment for selective patient populations with acute, cancer related, and chronic non-cancer pain. The purpose of these guidelines is to provide information for primary care physicians and other healthcare providers about the current use of opioids in pain management.

This Guideline attempts to define principles of practice that should produce high-quality patient care. It focuses on the needs of primary care practice but also is applicable to providers at all levels.

This Guideline should not be considered exclusive of other methods of care reasonably directed at obtaining the same results. The ultimate judgment concerning the propriety of any course of conduct must be made by the clinician after consideration of each individual patient situation.



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